

Proposed Revised Claims for 1275/190

1. (once amended) A method of providing an iron oxide complex for administration to a mammalian subject, the method [~~comprising~~] consisting of:
producing a carboxyalkylated reduced polysaccharide iron oxide complex; and
sterilizing the complex by autoclaving.
2. (no change) A method according to claim 1, wherein the reduced polysaccharide is a reduced polymer of glucose.
3. (no change) A method according to claim 2, wherein the reduced polymer of glucose is a reduced dextran.
4. (no change) A method according to claim 1, wherein the reduced polysaccharide is produced by reacting a polysaccharide with a reagent selected from the group consisting of: a borohydride salt, and hydrogen in the presence of an hydrogenation catalyst.
5. (cancel) A method of providing an iron oxide complex for administration to a mammalian subject, the method comprising:
producing a derivatized reduced polysaccharide iron oxide complex; and
sterilizing the complex by autoclaving.
6. (cancel) A method according to claim 5, wherein producing the complex includes derivatizing a reduced polysaccharide by carboxyalkylation.
7. (once amended) A method according to claim [6] 1, wherein [~~the carboxyalkylation is a carboxymethylation~~] producing the complex includes carboxyalkylating a reduced polysaccharide by carboxymethylation.
8. (no change) A method according to claim 7, wherein the reduced polysaccharide is a reduced dextran.
9. (no change) A method according to claim 8, wherein the administration to a mammalian subject is administration to a human.
10. (once amended) A method according to claim [5] 1, wherein the [~~derivatized~~] carboxyalkylated, reduced polysaccharide isolated as [~~the~~] a sodium salt does not contain an infrared absorption peak in the region of about 1650 cm^{-1} to about 1800 cm^{-1} .
11. (once amended) A method according to claim [5] 1, wherein producing the [~~derivatized~~] carboxyalkylated reduced polysaccharide is achieved at a temperature of less than about 50°C .

12. (once amended) A method according to claim 11, wherein producing the ~~[derivatized]~~ carboxyalkylated reduced polysaccharide is achieved at a temperature of less than about 40 °C.
13. A method according to claim ~~[5]~~ 1, wherein the iron oxide is superparamagnetic
18. A reduced polysaccharide iron oxide complex produced according to the method of claim 1, wherein the produced ~~[such]~~ complex ~~[being]~~ is stable at a temperature of at least 100 °C.
19. (once amended) A reduced polysaccharide iron oxide complex according to claim 18, ~~[such]~~ wherein the produced complex ~~[being]~~ is stable at a temperature of about 121 °C.
20. (once amended) A reduced polysaccharide iron oxide complex according to claim 19, ~~[such]~~ wherein the produced complex ~~[being]~~ is stable at a temperature of at least about 121 °C for a period of time effective to sterilize the complex.
21. (cancel) A reduced polysaccharide iron oxide complex according to claim 18, wherein the reduced polysaccharide is derivatized.
22. (once amended) A reduced polysaccharide iron oxide complex according to claim ~~[21]~~ 18, wherein the ~~[derivatized]~~ carboxyalkylated reduced polysaccharide is selected from the group consisting of a ~~[carboxyalkyl]~~ carboxymethyl, carboxyethyl and carboxypropyl reduced polysaccharide.
23. (cancel) A reduced polysaccharide iron oxide complex according to claim 22, wherein the carboxyalkyl is selected from the group consisting of carboxymethyl, carboxyethyl, and carboxypropyl.
24. (once amended) A reduced polysaccharide iron oxide complex according to claim ~~[23]~~ 22, wherein the reduced polysaccharide is a reduced dextran.
25. (once amended) A reduced polysaccharide iron complex according to claim 22, wherein the ~~[derivatized]~~ carboxyalkylated reduced dextran is a carboxymethyl reduced dextran.
26. (twice amended) A reduced polysaccharide iron oxide complex according to claim 24, wherein ~~[the amount of derivatization of]~~ the carboxyalkylated reduced dextran ~~[is]~~ comprises at least about 750 micromole of carboxyl groups per gram of polysaccharide.
27. (twice amended) A reduced polysaccharide iron oxide complex according to claim 26, wherein ~~[the level of derivatization of]~~ the carboxyalkylated reduced dextran ~~[is]~~ comprises at least about 900 micromole of carboxyl groups per gram of polysaccharide.

28. (twice amended) A reduced polysaccharide iron oxide complex according to claim 27, wherein ~~[the amount of derivatization of]~~ the carboxyalkylated reduced dextran ~~[is]~~ comprises at least about 1,10 micromole of carboxyl groups per gram of polysaccharide.

29. (twice amended) A reduced polysaccharide iron oxide complex according to claim [26] 28, wherein ~~[the amount of derivatization of]~~ the carboxyalkylated reduced dextran ~~[is]~~ comprises [at least] less than about 1,500 micromole of carboxyl groups per gram of polysaccharide~~[-, wherein said complex remains a colloidal suspension without substantial aggregation]~~ wherein said complex does not form substantial particulates.

35. (thrice amended) An improved method of administering to a mammalian subject a polysaccharide iron oxide complex ~~[of the type wherein there is a risk of edematous response]~~, wherein the improvement comprises ~~[utilizing for administration a derivatized]~~ administering a carboxyalkylated reduced polysaccharide [composition] iron oxide complex ~~[and in derivatizing the polysaccharide, providing]~~ having an extent of [derivatization] carboxyalkylation sufficient to produce decreased edematous response to the ~~[derivatized composition so that there is a decreased edematous response]~~ carboxyalkylated complex in comparison to ~~[utilizing a]~~ an edematous response to an administered polysaccharide that has not been thus ~~[derivatized]~~ carboxyalkylated.

36. (thrice amended) An improved method of administering to a mammalian subject a polysaccharide iron oxide complex wherein the ~~[composition includes]~~ polysaccharide in the complex is dextran ~~[of the type wherein there is a risk of edematous response]~~, wherein the improvement comprises ~~[utilizing for administration a carboxyalkylated]~~ administering a carboxymethylated reduced dextran [in lieu of dextran] iron oxide complex ~~[and in carboxymethylating the dextran, providing]~~ having an extent of carboxymethylation sufficient to produce decreased edematous response to the ~~[derivatized composition so that there is a decreased edematous response]~~ carboxymethylated complex in comparison to ~~[utilizing a]~~ an edematous response to an administered dextran that has not been thus ~~[derivatized]~~ carboxymethylated.

39 (twice amended) A method according to claim 36, further comprising sterilizing the ~~[composition]~~ complex by autoclaving.

40. (cancel) A method according to claim 39, wherein the subject is in need of a plasma extender.

41. (cancel) A method according to claim 36, further comprising providing a solution of an iron salt to form a carboxymethylated reduced dextran iron colloid formulation producing decreased edematous response.

42. (twice amended) A method according to claim [41] 36, further comprising sterilizing the carboxymethylated reduced dextran iron ~~[formulation]~~ oxide complex by autoclaving.

43. (no change) A method according to claim 42, wherein the subject is in need of iron.
44. (no change) A method according to claim 43, wherein the subject in need of iron is selected from the group of: a cancer patient, a gastroenteritis patient, and an erythropoietin recipient.
45. (thrice amended) A method of magnetic resonance imaging (MRI) according to claim ~~[41 of magnetic resonance imaging (MRI)]~~ 36 of the type including a reduced polysaccharide[-derived] iron oxide MRI contrast agent, ~~[wherein there is a risk of edematous response]~~, wherein the improvement comprises administering to the subject an effective dose of the contrast agent to ~~[obtain]~~ facilitate magnetic resonance imaging (MRI) of a tissue or organ ~~[so that]~~ wherein there is a decreased edematous response in comparison to [utilizing] an edematous response when an unmodified polysaccharide contrast agent is administered.
46. (twice amended) A method of magnetic resonance imaging according to claim 45, wherein the improvement further comprises administering ~~[an effective dose of the agent to obtain an MRI, followed within a single clinical visit by administering a further effective dose, to obtain a further MRI]~~ successive effective doses of the contrast agent to facilitate successive magnetic resonance imaging of a tissue or organ.
47. (once amended) A method according to ~~[either of claims 46]~~ claim 45, wherein the effective dose is about 0.1 to about 4.0mg of iron per kg of body weight of the subject.
48. (no change) A method according to claim 47, wherein the effective dose is about 0.2 to about 0.6 mg of iron per kg of body weight.
49. (no change) A method according to claim 47, wherein the effective dose is about 0.4 to about 1.0 mg of iron per kg of body weight.
50. (no change) A method according to claim 47, wherein the effective dose is about 1.0 to about 4.0 mg of iron per kg of body weight.
51. (once amended) A method according to claim 46, wherein the ~~[interval between administering]~~ successive effective doses ~~[and administering the further effective dose is]~~ are administered less than one hour apart.
52. (once amended) A method according to claim 51, wherein the ~~[interval between administering]~~ successive effective doses ~~[and administering the further effective dose is]~~ are administered less than thirty minutes apart.
53. (no change) A method of providing a contrast agent for in vivo MRI of a subject, comprising the steps of:
formulating a composition which is a carboxymethylated reduced coated
ultrasmall superparamagnetic iron oxide colloid; and

terminally sterilizing the composition by autoclaving.

54. (no change) A method of providing a hematinic agent for treating a subject deficient in iron, comprising the steps of:

formulating a composition which is a carboxymethylated reduced coated ultrasmall iron oxide colloid; and

terminally sterilizing the composition by autoclaving.

55. (no change) A method according to claim 53 or 54, having the further step of providing the autoclaved composition in a unit dosage.

56. (cancel) A kit containing multiple dosages of [the] an agent prepared by the method of claim 55.

57. (twice amended) An improved method of the type for administering a pharmacological polysaccharide composition ~~[for pharmacological use from a polysaccharide wherein there is a risk of edematous response]~~, wherein the improvement comprises prior to administering:

reducing ~~[and carboxylating]~~ the polysaccharide; and

[in] carboxylating[, providing] to an extent [of carboxylation] sufficient to produce a decreased edematous response to the [obtained carboxyalkylated] administered polysaccharide composition in comparison to [method for providing a] an edematous response to an administered unreduced uncarboxyalkylated polysaccharide [composition for pharmacological use obtained from an unmodified polysaccharide].

58. (once amended) A method according to claim 57, wherein the ~~[pharmacological use is in vivo administration]~~ method further comprises:

administering the reduced carboxyalkylated pharmacological polysaccharide composition to a mammalian subject as a plasma extender.

59. (once amended) An improved method of the type for obtaining a composition for pharmacological use from a dextran, wherein the improvement comprises:

reducing ~~[and carboxymethylating]~~ the dextran; and,

[in] carboxymethylating the dextran[, providing] to provide an extent of carboxymethylation sufficient to produce decreased edematous response to the [obtained carboxymethylated] administered dextran composition in comparison to [a method for obtaining a] an edematous response to an administered unreduced uncarboxyalkylated polysaccharide [composition for pharmacological use from an unmodified dextran].

60. (once amended) A method according to claim [59] 57, having the further step ~~[after the reacting step,]~~ of sterilizing the ~~[carboxymethylated]~~ carboxyalkylated reduced dextran composition.

61. (no change) A method according to claim 60, having the further step after the sterilizing step of providing the sterile composition as a single dosage unit.

62. (no change) A method according to claim 60, having the additional step of administering the composition to a mammal in need of a plasma extender.

63. (no change) A product for use as a plasma extender produced by the improved method of claim 60.

64. (once amended) A reduced [~~derivatized~~] carboxyalkylated polysaccharide iron oxide complex which is stable at a temperature of about 121 °C, wherein [the] a sodium salt of the complex does not contain an infrared absorption peak in the region of about 1650 cm^{-1} to about 1800 cm^{-1} .

65. (cancel) A reduced derivatized polysaccharide iron oxide complex according to claim 64, wherein the polysaccharide is carboxyalkylated.

66. (once amended) A reduced [~~derivatized~~] carboxyalkylated polysaccharide iron oxide complex according to claim 64, wherein the polysaccharide is [~~carboxyalkylated~~] carboxymethylated.

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